

86

Poster

# Diffusion-weighted Imaging Reflects Pathological Therapeutic Response and Predicts Relapse in Breast Cancer

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**Background:** Conventional imaging does not always accurately depict the pathological response to neoadjuvant chemotherapy (NAC). Diffusion-weighted (DW) magnetic resonance imaging (MRI) may provide additional insight into the chemotherapeutic effect. This study assessed whether the apparent diffusion coefficient (ADC) correlated with pathological outcome and prognosis in breast cancer patients receiving NAC.

**Materials and Methods:** Fifty-six patients with locally advanced breast cancer received surgery after NAC. Contrast enhanced and DW MRI was performed before and after NAC. Tumor response was assessed by change in ADC and it was compared with change in size. The pathological response was classified into five categories from mild response to complete response according to amount of residual cancer. The correlation between MRI parameters and postoperative pathologic findings was determined and the prognostic significance of ADC was also assessed.

**Results:** The overall clinical response rate after completion of the NAC regimen was 78.6%.

The distribution of the pathological response classification was as follows: Grade 0 (no response), 3 cases; Grade 1a (mild response), 22 cases; Grade 1b (moderate response), 12 cases; Grade 2 (marked response), 10 cases; Grade 3 (complete response), 8 cases. The ADC of primary breast lesions before NAC did not show a significant correlation with the pathological response. However, the ADC of primary breast lesions after NAC significantly increased and showed a linear trend with the pathological response. The correlation coefficients between the pathological response and ADC measured before and after chemotherapy were -0.09 and 0.64, respectively. The pathological response grade was correlated with percentage change in ADC value and the percentage change of the longest diameter on CE-MRI. The change in tumor size only showed a significant difference between grade 0 and 3, and between 1a and 3. However, the change in ADC showed a significant difference not only between those groups but also between 0 and 2, and between 1a and 2.

The correlation coefficients were 0.67 and 0.58 for change in ADC and change in tumor size, respectively. The change in ADC showed the strongest correlation coefficient of the four measured MRI parameters. The prognostic significance of the change in ADC was assessed with the cutoff value set at the median value (+26%). During a mean follow-up of 41 months, the higher ADC change group showed a significantly better prognosis than the lower ADC change group ( $p = 0.038$ ).

**Conclusions:** A change in ADC after chemotherapy could reflect the pathological response more accurately than the change in tumor size measured by CE-MRI. A reduced change in ADC was also significantly correlated with early relapse. Applying ADC values to evaluate the therapeutic effect, DW-MRI may help to identify breast cancer patients who have good prognosis and who may be able to avoid additional intervention.

87

Poster

# Comparison of 3-dimensional Synchrotron Radiation Micro-computed Tomographic Images of Breast Cancer Tissue with Serially Sectioned Their Corresponding Pathologic Slide Findings

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**Background:** Synchrotron radiation micro-computed tomography (SRμCT) is proved to be a promising method for diagnosis of breast diseases including malignancies due to its excellent spatial resolution and low radiation exposure. The purpose of this study was to demonstrate that high-spatial resolution synchrotron tomography can substantially improve the radiographic contrast of breast tissue in vitro when compared with that attained by using conventional mammography and CT. We imaged some breast tissue samples that were removed surgically from breast cancer patients. And the correspondence between tomographic images and their histopathological findings were determined.

**Material and Methods:** Experiments were performed at the bending magnet beamline 7B2 of Pohang Light Source (PLS) in Pohang Accelerator Laboratory (PAL), South Korea. All tissues were routinely fixed in 10%

neutral buffered formalin, and each sample was processed, rapidly frozen with dry ice, mounted on a computer-controlled precision stage and maintained at cryogenic temperature throughout data collection. Using white beam imaging system, 1,000 images were collected at 0.18° increments through 180°. The X-ray shadow of the specimen was converted into a visual image on scintillation crystal (CdWO<sub>4</sub>), magnified using a X20 objective microscope and captured using a digital CCD camera. The spatial resolution determined by standard sample was 1.5 μm. After imaging, the samples were embedded in paraffin, split into several sections and stained with hematoxylin and eosin. Obtained tomographic images were compared with corresponding histopathological findings in optical microscopy. A total of 1000 tomographic images were acquired from each sample, and only a small number of different typical cases were selected for a detailed analysis.

**Results:** Synchrotron tomographic images yield high contrast from smoothly varying internal structures corresponding to actual structures seen at histopathological analysis. The overall configuration of fibrous and adipose tissue is well correlated in between synchrotron tomogram and histologic section. And the improved visibility of mammographically indistinguishable lesions in vitro suggests that synchrotron tomography may be a valuable method in radiographic evaluation of the various breast lesions. Furthermore, various structures of breast cancer tissue at different levels were seen in a series of images unlike projected 2-dimensional image such as mammography.

**Conclusions:** In this study, tomography with SRμCT shows superior visualization of subject contrast, together with depth localization. The results suggest that tomography with SRμCT has potential as a diagnostic tool in breast imaging. But additional studies are needed for improved imaging and clinical applications.

88

Poster

# Referral Patterns for Older Patients with Suspected Breast Cancer in Nursing Homes

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**Background:** Many studies have addressed the care for older breast cancer patients in hospitals and cancer clinics. However, little is known about the extent of non-referral of frail elderly patients with suspected breast cancer in nursing homes.

**Methods:** A web-based survey was sent to all 1238 elderly care physicians (ECPs, registered at the National Association of Elderly Care Physicians and Social Geriatricians) who provide the primary care for nursing home patients. The survey inquired about their experiences with suspected breast cancer and subsequent choices regarding referral.

**Results:** Response rate was 34% (414/1238). Of the respondents, 60% of ECPs stated they had encountered at least one patient with suspected breast cancer in the past year. Of these, 33% reported not referring one or more patients. Patients not referred were older (median age 86 vs. 82 years), although some unreferred patients were as young as 60 years. Over 99% of physicians discussed their decision on referral with at least one other party (54 % with the patient, 87 % with a family member and 9% with another ECP). The motivation for choosing to refer patients to hospital were primarily the desire to confirm the diagnosis (28%), good general health and life-expectancy (19%), the fear of future ulceration or metastases (21%), and patient's preference for referral (18%). The primary reason stated for not referring was end-stage dementia (57%). Other reasons were the preferences of patient and/or family (29%), limited life-expectancy (23%), poor functional status or somatic comorbidity (18 and 16%, respectively) and advanced age in 8%.

**Conclusion:** The present survey shows that over 33% of nursing home patients with suspected breast cancer are not referred, in particular those with advanced dementia and poor functional status, because the referral process was thought to be too burdensome in comparison to the benefit. As the combination of dementia and suspected breast cancer is expected to double in the coming decades, now is the time to start thinking of better ways to organize cancer care for this vulnerable group of patients.